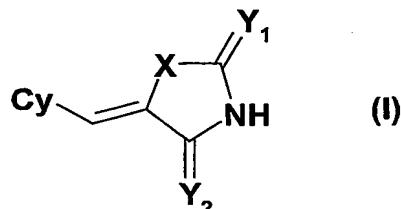


Claims

1. Process for improving the fertilization activity of spermatozoa, in particular for increasing spermatozoa motility, comprising the step of treating spermatozoa with a compound of formula (I)



5

as well as its geometrical isomers, its optically active forms as enantiomers, diastereomers and its racemate forms, as well as pharmaceutically acceptable salts and pharmaceutically active derivatives thereof, wherein

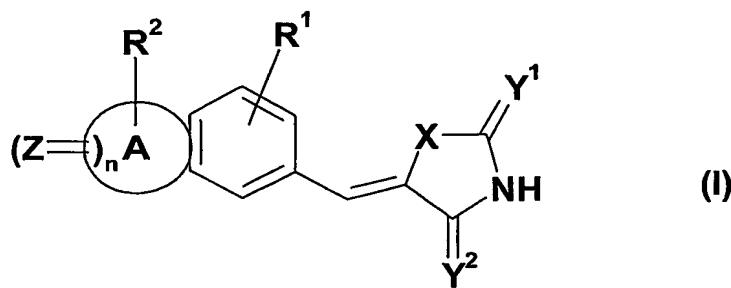
X is S, O or NH;

10

Y¹ and Y² are independently S, O or -NH;

Cy is a 5 to 8 membered carbocyclic or heterocyclic group may be fused with an aryl, heteroaryl, cycloalkyl or heterocycloalkyl group.

2. Process according to claim 1, whereby the compound has formula (I')



A is a 5-8 membered heterocyclic or carbocyclic group, wherein said carbocyclic group may be fused with aryl, heteroaryl, cycloalkyl or heterocycloalkyl;

X is S, O or NH;

Y¹ and Y² are independently S, O or -NH;

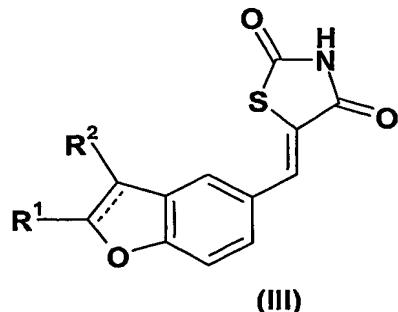
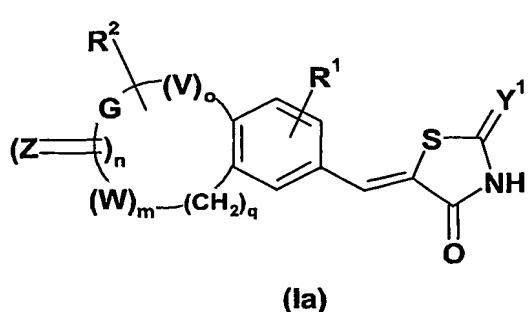
5 Z is S or O;

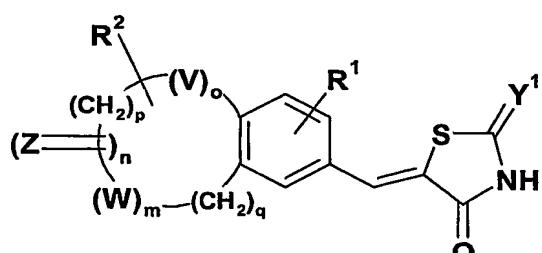
R¹ is H, CN, carboxy, acyl, C₁-C₆-alkoxy, halogen, hydroxy, acyloxy, C₁-C₆-alkyl carboxy, C₁-C₆-alkyl acyloxy, C₁-C₆-alkyl alkoxy, alkoxycarbonyl, C₁-C₆-alkyl alkoxycarbonyl, aminocarbonyl, C₁-C₆-alkyl aminocarbonyl, acylamino, C₁-C₆-alkyl acylamino, ureido, C₁-C₆-alkyl ureido, amino, C₁-C₆-alkyl amino, ammonium, sulfonyloxy, C₁-C₆-alkyl sulfonyloxy, sulfonyl, C₁-C₆-alkyl sulfonyl, sulfinyl, C₁-C₆-alkyl sulfinyl, sulfanyl, C₁-C₆-alkyl sulfanyl, sulfonylamino, C₁-C₆-alkyl sulfonylamino or carbamate;

10 R² is selected from the group comprising or consisting of H, halogen, acyl, amino, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, C₁-C₆-alkyl carboxy, C₁-C₆-alkyl acyl, C₁-C₆-alkyl alkoxycarbonyl, C₁-C₆-alkyl aminocarbonyl, C₁-C₆-alkyl acyloxy, C₁-C₆-alkyl acylamino, C₁-C₆-alkyl ureido, C₁-C₆-alkyl amino, C₁-C₆-alkyl alkoxy, C₁-C₆-alkyl sulfanyl, C₁-C₆-alkyl sulfinyl, C₁-C₆-alkyl sulfonyl, C₁-C₆-alkyl sulfonylaminoaryl, aryl, C₃-C₈-cycloalkyl or heterocycloalkyl, C₁-C₆-alkyl aryl, C₂-C₆-alkenyl-aryl, C₂-C₆-alkynyl aryl, carboxy, cyano, hydroxy, C₁-C₆-alkoxy, nitro, acylamino, ureido, C₁-C₆-alkyl carbamate, sulfonylamino, sulfanyl, or sulfonyl;

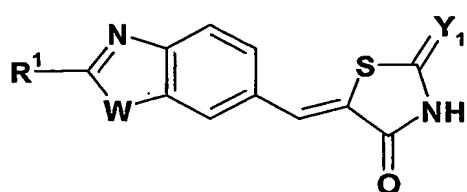
15 n is 0, 1 or 2.

20 3. Process according to claim 1 or 2, wherein the compound is selected from any of formulae (Ia), (Ib), (Ic) or (Id)

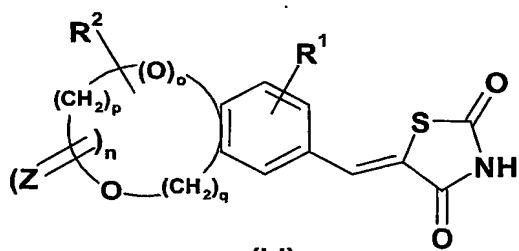




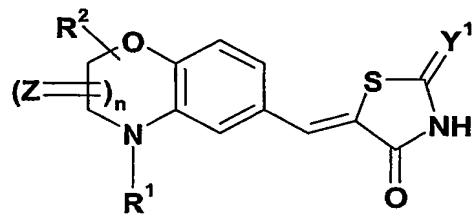
(Ib)



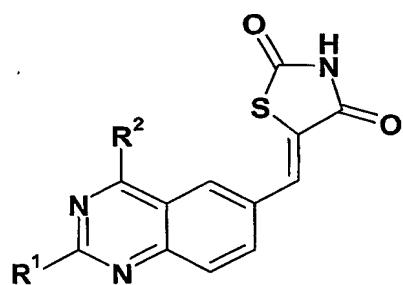
(Ic)



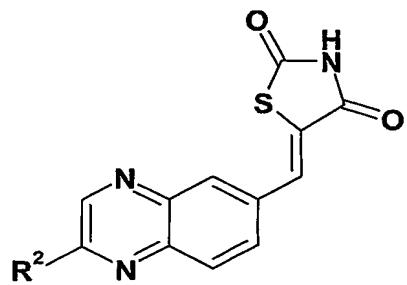
(Id)



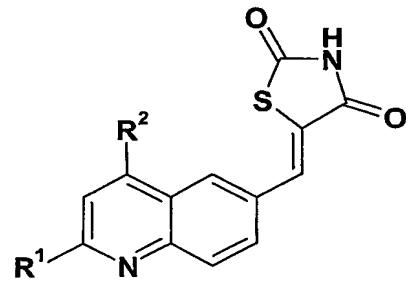
(II)



(IV)



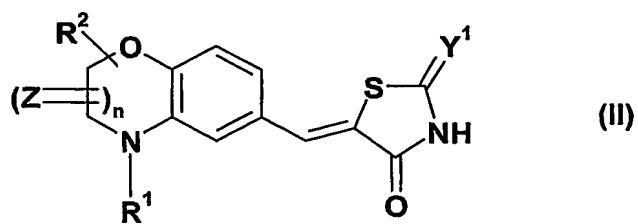
(V)



(VI)

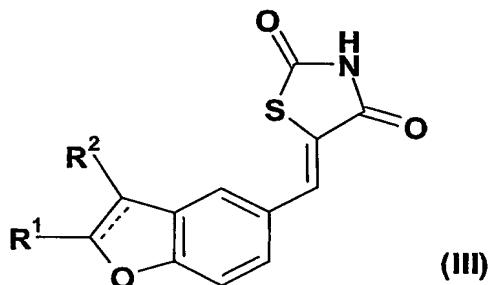
wherein R¹, R², Y¹, Z and n are as above-defined, G is a C₁-C₅ alkylene or a C₁-C₅ alkenylene group, W and V are each independently from each other selected from O, S, -NR³ wherein R³ is H or a C₁-C₆ alkyl group, m, n and o are each independently from each other 0 or 1, p and q are independently from each other an integer from 1 to 4.

4. Process according to any of the preceding claims, wherein the compound has formula (II)



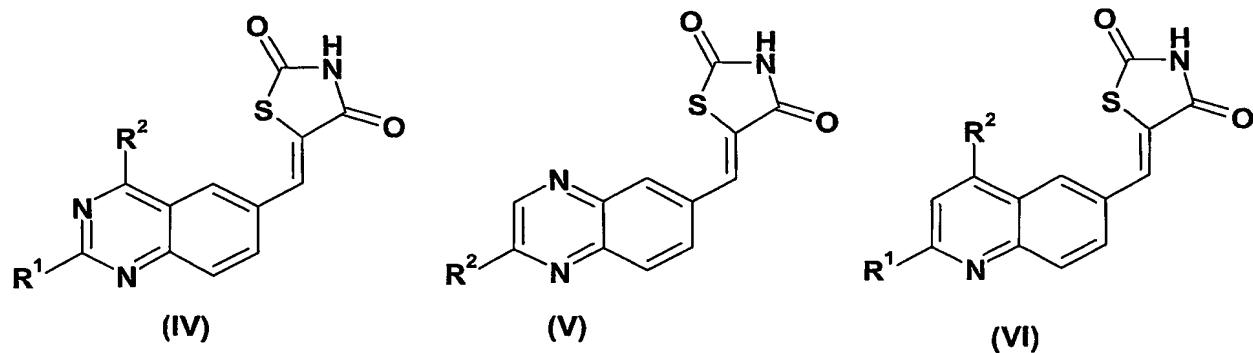
wherein Z, Y¹, R¹, R² are as above defined; n is 0 or 1.

5. Process according to any of claims 1 to 3, wherein the compound has formula (III)



5 wherein R^1 and R^2 are as above defined.

6. Process according to any of claims 1 to 3, wherein the compound has any of formulae (IV), (V) or (VI);



wherein R^1 and R^2 are as above defined.

.0 7. Process according to any of claims 1 to 6, wherein treating the spermatozoa with the compound of formula (I) is performed on seminal liquid comprising the spermatozoa.

8. Process according to any of claims 1 to 7, further comprising separating the spermatozoa by spermatozoa separation methods used in assisted reproduction techniques.
9. Process according to claim 8, wherein separating the spermatozoa is performed by a method selected from the wash and spin method, the sedimentation method, the direct swim-up method, the pellet and swim-up method, the buoyant density gradient method.
5
10. Process according to claim 9, wherein separating the spermatozoa is performed by the direct swim-up method.
11. Process according to any of the preceding claims, wherein the process is performed on mammal spermatozoa, in particular on human spermatozoa.
10
12. Process according to any of the preceding claims, wherein the compound of formula (I) is selected from the group consisting of :
 - 5-(1,3-benzodioxol-5-ylmethylene)-1,3-thiazolidine-2,4-dione
 - 5-(1,3-benzodioxol-5-ylmethylene)-2-thioxo-1,3-thiazolidin-4-one
 - 5-(2,3-dihydro-1,4-benzodioxin-6-ylmethylene)-1,3-thiazolidine-2,4-dione
 - 5-(2,3-dihydro-1-benzofuran-5-ylmethylene)-1,3-thiazolidine-2,4-dione
 - 5-[(7-methoxy-1,3-benzodioxol-5-yl)methylene]-1,3-thiazolidine-2,4-dione
 - 5-[(9,10-dioxo-9,10-dihydroanthracen-2-yl)methylene]-1,3-thiazolidine-2,4-dione
 - (5-[(2,2-difluoro-1,3-benzodioxol-5-yl)methylene]-1,3-thiazolidine-2,4-dione
 - (5Z)-5-(1,3-dihydro-2-benzofuran-5-ylmethylene)-1,3-thiazolidine-2,4-dione
 - 5-(1-benzofuran-5-ylmethylene)-1,3-thiazolidine-2,4-dione
 - 5-[(4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-6-yl)methylene]-1,3-thiazolidine-2,4-dione
 - 5-(1,3-benzodioxol-5-ylmethylene)-2-imino-1,3-thiazolidin-4-one
 - 5-Quinolin-6-ylmethylene-thiazolidine-2,4-dione
 - 5-Quinolin-6-ylmethylene-2-thioxo-thiazolidin-4-one

2-Imino-5-quinolin-6-ylmethylene-thiazolidin-4-one

5-(3-Methyl-benzo[d]isoxazol-5-ylmethylene)-thiazolidine-2,4-dione

5-(4-Phenyl-quinazolin-6-ylmethylene)-thiazolidine-2,4-dione

5-(4-Dimethylamino-quinazolin-6-ylmethylene)-thiazolidine-2,4-dione

5-[(4-aminoquinazolin-6-yl)methylene]-1,3-thiazolidine-2,4-dione

5-[(4-piperidin-1-ylquinazolin-6-yl)methylene]-1,3-thiazolidine-2,4-dione

5-[(4-morpholin-4-ylquinazolin-6-yl)methylene]-1,3-thiazolidine-2,4-dione

5-{{[4-(benzylamino)quinazolin-6-yl]methylene}-1,3-thiazolidine-2,4-dione

5-{{[4-(diethylamino)quinazolin-6-yl]methylene}-1,3-thiazolidine-2,4-dione

5-{{4-[(pyridin-2-ylmethyl)amino]quinazolin-6-yl}methylene}-1,3-thiazolidine-2,4-dione

5-{{4-[(pyridin-3-ylmethyl)amino]quinazolin-6-yl}methylene}-1,3-thiazolidine-2,4-dione

ethyl 1-{6-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]quinazolin-4-yl}piperidine-3-carboxylate

ethyl 1-{6-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]quinazolin-4-yl}piperidine-4-carboxylate

tert-butyl 1-{6-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]quinazolin-4-yl}-L-proline

5-{{[4-(4-methylpiperazin-1-yl)quinazolin-6-yl]methylene}-1,3-thiazolidine-2,4-dione

5-{{[4-(4-pyrimidin-2-ylpiperazin-1-yl)quinazolin-6-yl]methylene}-1,3-thiazolidine-2,4-dione

5-{{4-[4-(4-fluorophenyl)piperidin-1-yl]quinazolin-6-yl}methylene}-1,3-thiazolidine-2,4-dione

5-{{[4-(4-benzylpiperidin-1-yl)quinazolin-6-yl]methylene}-1,3-thiazolidine-2,4-dione

5-{{4-[4-(2-phenylethyl)piperidin-1-yl]quinazolin-6-yl}methylene}-1,3-thiazolidine-2,4-dione

5-{{[4-(4-methylpiperidin-1-yl)quinazolin-6-yl]methylene}-1,3-thiazolidine-2,4-dione

5-{{[4-(4-hydroxypiperidin-1-yl)quinazolin-6-yl]methylene}-1,3-thiazolidine-2,4-dione

1-[6-(2,4-Dioxo-thiazolidin-5-ylidenemethyl)-quinazolin-4-yl]-piperidine-4-carboxylic acid

1-[6-(2,4-Dioxo-thiazolidin-5-ylidenemethyl)-quinazolin-4-yl]-piperidine-3-carboxylic acid

1-[6-(2,4-Dioxo-thiazolidin-5-ylidenemethyl)-quinazolin-4-yl]-pyrrolidine-2-carboxylic acid

5-(4-Methylamino-quinazolin-6-ylmethylene)-thiazolidine-2,4-dione

5-(4-Methoxy-quinazolin-6-ylmethylene)-thiazolidine-2,4-dione

2-Imino-5-(4-methylamino-quinazolin-6-ylmethylene)-thiazolidin-4-one

2-Imino-5-(4-piperidine-quinazolin-6-ylmethylene)-thiazolidin-4-one

2-Imino-5-(4-dimethylamino-quinazolin-6-ylmethylene)-thiazolidin-4-one

5-(2-Methyl-2H-benzotriazol-5-ylmethylene)-thiazolidine-2,4-dione

5-(3-Methyl-3H-benzotriazol-5-ylmethylene)-thiazolidine-2,4-dione

5-(3-Ethyl-3H-benzoimidazol-5-ylmethylene)-thiazolidine-2,4-dione

5-{{1-(4-phenylbutyl)-1H-benzimidazol-6-yl]methylene}-1,3-thiazolidine-2,4-dione

5-[(1-prop-2-yn-1-yl-1H-benzimidazol-6-yl)methylene]-1,3-thiazolidine-2,4-dione

5-[(1-{2-[4-(trifluoromethyl)phenyl]ethyl}-1H-benzimidazol-6-yl)methylene]-1,3-thiazolidine-2,4-dione

5-({1-[2-(4-hydroxyphenyl)ethyl]-1H-benzimidazol-6-yl}methylene)-1,3-thiazolidine-2,4-dione

methyl 4-{{6-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1H-benzimidazol-1-yl}cyclohexanecarboxylate}

5-({1-[2-(5-methoxy-1H-indol-3-yl)ethyl]-1H-benzimidazol-6-yl}methylene)-1,3-thiazolidine-2,4-dione

5-({1-[(1-methyl-1H-pyrazol-4-yl)methyl]-1H-benzimidazol-6-yl}methylene)-1,3-thiazolidine-2,4-dione

5-({1-[2-(3,4-dimethoxyphenyl)ethyl]-1H-benzimidazol-6-yl}methylene)-1,3-thiazolidine-2,4-dione

5-({1-[2-(4-phenoxyphenyl)ethyl]-1H-benzimidazol-6-yl}methylene)-1,3-thiazolidine-2,4-dione

5-({1-[4-(trifluoromethyl)benzyl]-1H-benzimidazol-6-yl}methylene)-1,3-thiazolidine-2,4-dione

4-{{6-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1H-benzimidazol-1-yl}cyclohexanecarboxylic acid}

5-[(1-isobutyl-1H-benzimidazol-6-yl)methylene]-1,3-thiazolidine-2,4-dione
5-(1-[2-(1,3-benzodioxol-4-yl)ethyl]-1H-benzimidazol-6-yl)methylene)-1,3-thiazolidine-2,4-dione
5-(1-[2-(2-phenoxyphenyl)ethyl]-1H-benzimidazol-6-yl)methylene)-1,3-thiazolidine-2,4-dione
5-{[1-(3,3-diphenylpropyl)-1H-benzimidazol-6-yl]methylene}-1,3-thiazolidine-2,4-dione
5-{[1-(2-methoxybenzyl)-1H-benzimidazol-6-yl]methylene}-1,3-thiazolidine-2,4-dione

5-{[1-(3-furylmethyl)-1H-benzimidazol-6-yl]methylene}-1,3-thiazolidine-2,4-dione
5-[(1-propyl-1H-benzimidazol-6-yl)methylene]-1,3-thiazolidine-2,4-dione
5-Quinoxalin-6-ylmethlene-thiazolidine-2,4-dione
5-Quinoxalin-6-ylmethlene-2-thioxo-thiazolidin-4-one
2-Imino-5-quinoxalin-6-ylmethlene-thiazolidin-4-one
5-Benzothiazol-6-ylmethlene-thiazolidine-2,4-dione
5-(3-Methyl-benzofuran-5-ylmethlene)-thiazolidine-2,4-dione
5-(2-Bromo-3-methyl-benzofuran-5-ylmethlene)-thiazolidine-2,4-dione
5-(3-bromo-benzofuran-5-ylmethlene)-thiazolidine-2,4-dione

3-[5-(2,4-Dioxo-thiazolidin-5-ylidenemethyl)-benzofuran-3-yl]-acrylic acid ethyl ester
3-[5-(2,4-Dioxo-thiazolidin-5-ylidenemethyl)-benzofuran-3-yl]-acrylic acid
5-[3-(3-Oxo-3-piperidin-1-yl-propenyl)-benzofuran-5-ylmethlene]-thiazolidine-2,4-dione
Methyl 1-((3-{5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1-benzofuran-3-yl}prop-2-enoyl)proline
Methyl 1-((3-{5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1-benzofuran-3-yl}prop-2-enoyl)-D-proline
(5-(3-[3-oxo-3-pyrrolidin-1-ylprop-1-en-1-yl]-1-benzofuran-5-yl)methylene)-1,3-thiazolidine-2,4-dione
5-(3-[3-morpholin-4-yl-3-oxoprop-1-en-1-yl]-1-benzofuran-5-yl)methylene)-1,3-thiazolidine-2,4-dione
Methyl 1-(3-{5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1-benzofuran-3-yl}prop-2-enoyl)-L-proline

N-cyclohexyl-3-{5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1-benzofuran-3-yl}-N-methylacrylamide

3-{5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1-benzofuran-3-yl}-N-ethyl-N-(2-hydroxyethyl)acrylamide

N-cyclobutyl-3-{5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1-benzofuran-3-yl}acrylamide

5-({3-[3-azetidin-1-yl-3-oxoprop-1-en-1-yl]-1-benzofuran-5-yl}methylene)-1,3-thiazolidine-2,4-dione

5-({3-[3-(1,3-dihydro-2H-isoindol-2-yl)-3-oxoprop-1-en-1-yl]-1-benzofuran-5-yl}methylene)-1,3-thiazolidine-2,4-dione

5-({3-[3-azepan-1-yl-3-oxoprop-1-en-1-yl]-1-benzofuran-5-yl}methylene)-1,3-thiazolidine-2,4-dione

3-{5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1-benzofuran-3-yl}-N-piperidin-1-ylacrylamide

3-{5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1-benzofuran-3-yl}-N-(pyridin-3-ylmethyl)acrylamide

N-cyclohexyl-3-{5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1-benzofuran-3-yl}acrylamide

5-({3-[3-(4-methylpiperazin-1-yl)-3-oxoprop-1-en-1-yl]-1-benzofuran-5-yl}methylene)-1,3-thiazolidine-2,4-dione

N-cycloheptyl-3-{5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1-benzofuran-3-yl}acrylamide

5-({3-[3-(2,5-dihydro-1H-pyrrol-1-yl)-3-oxoprop-1-en-1-yl]-1-benzofuran-5-yl}methylene)-1,3-thiazolidine-2,4-dione

N-cyclopentyl-3-{5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-1-benzofuran-3-yl}acrylamide

3-[5-(2,4-Dioxo-thiazolidin-5-ylidenemethyl)-benzofuran-3-yl]-propionic acid ethyl ester

3-[5-(2,4-Dioxo-thiazolidin-5-ylidenemethyl)-benzofuran-3-yl]-propionic acid

5-[3-(3-Oxo-3-piperidin-1-yl-propyl)-benzofuran-5-ylmethylene]-thiazolidine-2,4-dione

6-(2,4-Dioxo-thiazolidin-5-ylidenemethyl)-2,3-dihydro-benzo[1,4]oxazine-4-carboxylic acid tert-butyl ester

5-(3,4-Dihydro-2H-benzo[1,4]oxazin-6-ylmethylene)-thiazolidine-2,4-dione

5-(4-Benzoyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-ylmethylene)-thiazolidine-2,4-dione

5-(4-Acetyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-ylmethylene)-thiazolidine-2,4-dione
6-(2,4-Dioxo-thiazolidin-5-ylidenemethyl)-benzo[1,4]oxazine-4-carboxylic acid tert-butyl ester

[6-(2,4-Dioxo-thiazolidin-5-ylidenemethyl)-3-oxo-2,3-dihydro-benzo[1,4]-oxazin-4-yl]-acetic acid methyl ester

N-Benzyl-2-[6-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-3-oxo-2,3-dihydro-benzo[1,4]oxazin-4-yl]-acetamide

5-(4-Butyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-ylmethylene)-thiazolidine-2,4-dione

5-(4-Benzyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-ylmethylene)-thiazolidine-2,4-dione

5-(2-Chloro-benzofuran-5-ylmethylene)-thiazolidine-2,4-dione

5-(3-Amino-benzo[d]isoxazol-5-ylmethylene)-thiazolidine-2,4-dione

5-(3-Phenylethynyl-benzofuran-5-ylmethylene)-thiazolidine-2,4-dione

5-Benzo[1,2,5]thiadiazol-5-ylmethylene-thiazolidine-2,4-dione

5-Benzo[1,2,5]oxadiazol-5-ylmethylene-thiazolidine-2,4-dione

5-(2-Methyl-benzofuran-6-ylmethylene)-thiazolidine-2,4-dione

5-(2-Carboxymethyl-benzofuran-6-ylmethylene)-thiazolidine-2,4-dione

5-(3-Bromo-2-fluoro-2,3-dihydro-benzofuran-6-ylmethylene)-thiazolidine-2,4-dione

5-(2-Fluoro-benzofuran-6-ylmethylene)-thiazolidine-2,4-dione

13. Process according to any of the preceding claims, wherein said spermatozoa are treated with an amount of a compound of formula (I) in the range of about 0.01 to 1000 μM , about 5 to 500 μM , or about 10 to 100 μM .

14. Process according to any of the preceding claims, wherein treating the spermatozoa with a compound of formula (I) comprises incubating the spermatozoa for a period of

time in the range of about 30 minutes to 10 hours or about 1 to 8 hours or about 2 to 6 hours at a temperature of around 37°C.

15. Spermatozoa obtainable by the process according to any of claims 1 to 14.
16. Use of a compound according to formula (I) for improving the fertilization rate in assisted reproduction techniques.
5
17. Use according to claim 14, wherein the assisted reproduction techniques are selected from in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT), or intra-uterine insemination (IUI).
18. Use of a compound according to formula (I) for the preparation of a pharmaceutical composition for the treatment of infertility, in particular male infertility.
10
19. Use of a compound according to any of formula (I) for the preparation of a pharmaceutical composition for improving spermatozoa fertilization activity, in particular for increasing spermatozoa motility.
20. Method of ART therapy, comprising treating spermatozoa with a compound of any of
5 formulae (I) as above-defined.
21. Method according to claim 20, wherein said ART are selected from in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT), or intra-uterine insemination (IUI).
22. A medium for storage and/or transportation of spermatozoa comprising a compound of any of formula (I).
- 0 23. Medium according to claim 22 for the storage and/or transportation of mammal spermatozoa, in particular human spermatozoa.
24. Medium according to any of claims 22 or 23, comprising an amount of a compound of formula (I) in the range of about 0.01 to 1000 µM, about 5 to 500 µM, or about 10 to 100 µM.